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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/731,457	12/06/2000	Ian Popoff	RTS-0182	1220

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EXAMINER

SCHULTZ, JAMES

ART UNIT PAPER NUMBER

1635

DATE MAILED: 06/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

3M

Advisory Action

Application No.

09/731,457

Applicant(s)

POPOFF ET AL.

Examiner

J. Douglas Schultz, Ph.D.

Art Unit

1635

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 09 June 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☒ The period for reply expires 5 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) ☐ they raise the issue of new matter (see Note below);
 - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☐ Applicant's reply has overcome the following rejection(s): _____.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☒ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: _____.

Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.
10. ☐ Other: _____

Continuation of 5. does NOT place the application in condition for allowance because: applicants request for reconsideration merely re-states arguments that have been addressed in full in the final Office action mailed January 5, 2004. Furthermore, the affidavit submitted after final does not obviate the instant rejection because the arguments contained therein are not considered convincing. Although applicants have not submitted any reason why such arguments were not presented while prosecution was open, the affidavit has been considered and is addressed briefly below.

The affidavit, authored by an employee of the assignee, disputes the determination that one of ordinary skill in the art would find the instant invention obvious, that is antisense oligos directed to human damage specific DNA binding protein 1, p127 (DDB) that inhibit at least 60%. Applicants argue there is no motivation to make antisense targeted to DDB, because Dualan allegedly does not teach or suggest inhibitors to the DDB target. However, as stated in the Office action mailed in July 2003, one would have been motivated to make such compounds because Krishnamoorthy et al. teach antibody inhibition of DDB p127 as a means of testing the function of DDB p127, and because Hayes et al. teach that DDB p127 stimulates E2F1-activated transcription of cell-cycle related genes that are essential for DNA replication and cell cycle progression (page 246). Since Krishnamoorthy et al. teach the value of inhibiting the DDB p127 target as a means of understanding DDB p127 function, one of ordinary skill would have been motivated to make and use alternative inhibitors of DDB, such as the antisense inhibitors as taught by Taylor. Furthermore, because Hayes et al. teach that DDB regulates a gene that controls cell cycle progression, one would have been motivated to further characterize the function of DDB p127 as it pertains to undesirable cell-proliferation.

Applicants argue that it is not possible to predict whether any particular oligo will inhibit its target. However, applicants are referred to the claim language which does not claim any particular oligo, but rather the genus of oligos that inhibit to the 60% level. It is maintained that one would not need to predict what any one particular oligo will do if one can reasonably expect to find some that do inhibit to the claimed level.

Applicants appear to argue that there is no reasonable expectation of ever finding an antisense against a particular gene that inhibits to the 60% level, despite the peer-reviewed statements of Taylor that only 3-6 oligos need to be screened in order to find one that inhibits gene expression by 66-95% in vitro. Applicants have provided the results of antisense screens performed against two genes, which show that no oligos inhibited to the claimed 60% level. However, it is not at all clear that this is considered to be representative of the state of antisense technology. Indeed, a brief review of the first randomly chosen 10 patents issued to the assignee that published before applicants filing date (i.e. 6,001,992; 6,124,133; 6,133,031; 6,136,603; 6,140,124; 5,985,558; 6,020,199; 6,046,049; 6,133,032; and 6,140,126) reveals that every single one contains anywhere from a few to many oligos that inhibit over 60%. Thus, it is not clear whether applicants submission represents data that was picked and chosen for its results, or rather, indicates the state of the art as a whole. The review described above suggests that the data is not indicative of the state of the art as a whole.

Finally, it is noted that Baracchini indicates several antisense compounds capable of inhibiting its target at least 60%. Contrary to applicants indication, Taylor et al. does not purport to predict a priori whether a compound will inhibit its target, but rather narrows the field to indicates which oligos are likely to be successful when screened. The fact that Taylor et al. does not provide experimental detail indicating the conditions used does not mitigate the fact that such knowledge is available in the art, particularly in view of Baracchini et al., and the ten patents cited above, all of which indicate numerous oligos inhibiting to the 60% level, in addition to materials and methods and methods necessary to achieve such inhibition.

Accordingly, the submission of negative results from two selected genes is not considered to refute the numerous patents and peer-reviewed statements available to one of ordinary skill at the time of filing.

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